Gitelman Syndrome with Atypical Presentation: Severe Hypokalaemia and Hearing Loss in a Young Woman

Síndrome de Gitelman com Apresentação Atípica: Hipocaliemia Severa e Perda Auditiva em Mulher Jovem

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Abstract:

Gitelman syndrome (GS) is a rare autosomal recessive tubular disorder characterized by hypokalaemia with metabolic alkalosis, hypomagnesemia, and hypocalciuria, caused by mutations in the *SLC12A3* gene. Although it is not typically associated with hearing loss, it can overlap with Bartter phenotypes.

We report a 38-year-old woman with a history of sensorineural hearing loss presented to the emergency department with progressive weakness and paraesthesia. Laboratory tests showed severe hypokalaemia (2.1 mmol/L), metabolic alkalosis, and mild hypomagnesemia. Renal potassium and chloride wasting were demonstrated. Genetic testing revealed *SLC12A3* compound heterozygosity for two pathogenic variants, confirming Gitelman syndrome.

The coexistence of sensorineural hearing loss and findings compatible with Gitelman syndrome shows that there can exist a phenotypic overlap between tubular salt-wasting disorders. It is important to do a genetic test for accurate diagnosis and management.

Keywords: Gitelman Syndrome/diagnosis; Gitelman Syndrome/genetics; Hearing Loss, Sensorineural.

Resumo:

A síndrome de Gitelman é um distúrbio tubular autossómico recessivo raro caraterizado por hipocalemia com alcalose metabólica, hipomagnesemia e hipocalciúria causada por mutação no gene *SLC12A3*. Apesar de não se associar tipicamente a perda auditiva, pode haver sobreposição com os fenótipos de Bartter.

Apresentamos o caso de uma mulher de 38 anos com uma história de perda auditiva neurossensorial que recorreu ao serviço de urgência com fraqueza progressiva e parestesias. Analiticamente apresentava hipocaliemia (2,1 mmol/L), alcalose metabólica e hipomagnesemia ligeira. Apresentava potássio e cloro urinário aumentados. O teste genético revelou uma mutação no gene *SLC12A3* com duas mutações em heterozigotia.

A coexistência de surdez neurosensorial e achados compatíveis com síndrome de Gitelman revelam que pode existir a sobreposição entre patologias tubulures perdedoras de sal. É importante fazer um teste genético para um diagnóstico e gestão mais precisos.

Palavras-chave: Perda Auditiva Neurossensorial; Síndrome de Gitelman/diagnóstico; Síndrome de Gitelman/genética.

Learning Points

1. Gitelman syndrome should be considered in patients with hypokalemic metabolic alkalosis and hypomagnesemia.
2. Careful biochemical profiling, particularly hypomagnesemia and hypocalciuria, remains pivotal in distinguishing Gitelman syndrome from other salt-losing tubulopathies with overlapping clinical features.
3. Sensorineural hearing loss does not exclude the diagnosis of Gitelman syndrome and may lead to misclassification as Bartter syndrome in the absence of genetic confirmation.
4. Early recognition and appropriate management with electrolyte supplementation and potassium-sparing agents can result in good long-term outcomes.

Introduction

Gitelman syndrome is an autosomal recessive renal tubular disorder caused by mutations in *SLC12A3*, encoding the thiazide-sensitive sodium-chloride co-transporter (NCC) in the distal convoluted tubule.[1] It manifests as hypokalaemia, hypomagnesemia, metabolic alkalosis and hypocalciuria.

While Gitelman syndrome is classically distinguished from Bartter syndrome by its biochemical profile and later age of onset, atypical forms with overlapping features can exist.[2] Sensorineural hearing loss, although rare in Gitelman syndrome, is a hallmark of certain Bartter subtypes and may lead to some diagnostic confusion.[3]

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Case Report

A 38-year-old woman with a history of bilateral sensorineural hearing loss since adolescence presented in the emergency department with progressive fatigue, muscle weakness, and distal paraesthesia over several months. She denied vomiting, diarrhoea, or use of diuretics. There was no family history of renal disease or deafness.

On admission, she was normotensive (110/70 mmHg), with normal hydration status. Neurological examination without alterations.

Blood analysis revealed:

- Potassium: 2.5 mmol/L (3.5–5.0 mmol/L)
- Magnesium: 1.6 mg/dL (1.7–2.3 mg/dL)
- Chloride: 100 mmol/L
- Sodium: 139 mmol/L
- Creatinine: 0.8 mg/dL
- Arterial blood gas: metabolic alkalosis (pH 7.49; HCO_3^-30.5 mmol/L)

Urinary studies revealed increased potassium and chloride excretion (Na 78 mEq/L; K 35 mEq/L; Cl 105 mEq/L), compatible with a salt-losing tubulopathy. Urinary calcium was <50 mg/24h. Plasma renin and aldosterone levels were elevated (16 ng/mL/h and 69.8 ng/dL, respectively), consistent with secondary hyperaldosteronism.

An audiogram confirmed bilateral moderate-to-severe sensorineural hearing loss.

Differential diagnoses included Bartter and Gitelman syndrome. The absence of hypercalciuria and the biochemical pattern favoured GS.

Genetic testing (using Next Generation Sequencing) identified two pathogenic variants (c.1964G>A p.(*Arg655His*) and c.2549T>C p.(*Leuc850Pro*)) in *SLC12A3* gene in compound heterozygosity, confirming the diagnosis of Gitelman syndrome.

She maintained treatment with potassium chloride 1200 mg per os three times daily, spironolactone 100 mg *per os* once daily and magnesium sulfate 1229.6 mg *per os* twice daily. At 6-month follow-up, she remained asymptomatic, with stable levels of serum potassium and magnesium and no further episodes of muscle weakness or paraesthesia.

Discussion

The coexistence of sensorineural hearing loss in a patient with Gitelman syndrome represents an uncommon but clinically relevant diagnostic challenge.[4,5]

There are several overlapping features between Bartter syndrome and Gitelman syndrome. Bartter syndrome, particularly type IV, is commonly associated with sensorineural hearing loss and typically presents earlier in life, often during childhood, although the clinical severity can vary. However, classic Gitelman syndrome does not typically involve hearing loss, since *SLC12A3* mutations affect only the distal convoluted tubule. However, rare reports describe atypical Gitelman phenotypes with hearing loss, which can result of coexisting mutations or shared ion transport disturbances between renal and cochlear epithelia.[3]

This overlap highlights the functional interdependence of renal tubular and inner ear ion channels, emphasizing also the importance of genetic tests to distinguish between Gitelman syndrome and Bartter subtypes. In our patient, biochemical findings and genetic confirmation of *SLC12A3* mutations in compound heterozygosity supported the diagnosis of Gitelman syndrome.

Management principles remain similar—lifelong oral potassium and magnesium supplementation, potassium-sparing agents, and regular monitoring.[6] Early recognition and genotyping are essential for the right treatment and follow-up.

Conclusion

This case emphasizes the importance of genetic testing in differentiating between salt-losing tubulopathies. The coexistence of sensorineural hearing loss and biochemical findings consistent with Gitelman syndrome may mimic Bartter type IV, but genetic confirmation ensures accurate classification and targeted management. ■

Contributorship Statement

SFO, AB, IAM – Clinical Management of the patient. Literature review. Writing. Clinical revision.
NCP – Clinical management of the patient. Literature review. Writing.
JB – Literature review. Writing. Clinical revision. Final approval.

Declaração de Contribuição

SFO, AB, IAM – Gestão clínica do doente; revisão da literatura; redação do manuscrito; revisão clínica do manuscrito.
NCP – Gestão clínica do doente; revisão da literatura; redação do manuscrito.
JB – Revisão da literatura; redação do manuscrito; revisão clínica do manuscrito; aprovação final o manuscrito.

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